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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/667,096	09/18/2003	Brian R. MacDonald	PRD-2110-USANP	1638

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/667,096	MACDONALD ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-12 and 15-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-12 and 15-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 September 2003 and 01 February 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/16/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 12 March 2007 has been entered in full. Claims 2, 8-12, 15 are amended. Claims 1, 13-14 are cancelled. Claims 31-34 are added.

Claims 2-12 and 15-34 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The objection to the Figure 2 set forth at page 2 of the previous Office Action (03 August 2006) is *withdrawn* in view of the newly submitted Figure 2 (01 February 2007).

2. The objections to the specification as set forth at page 3 of the previous Office Action (03 August 2006) are *withdrawn* in view of the amended specification and Applicant's persuasive arguments (12 March 2007).

3. The objections to claims 2, 7-15, 20-21, and 26 as set forth at pages 3-4 of the previous Office Action (03 August 2006) are *withdrawn* in view of the amended and cancelled claims (12 March 2007).

4. The rejections of claims 2-30 under 35 U.S.C. § 112, second paragraph as set forth at pages 4-5 of the previous Office Action (03 August 2006) are *withdrawn* in view of the amended and cancelled claims (12 March 2007).

5. The rejection of claims 2-6 and 9-12 under 35 U.S.C. § 102(b) as set forth at pages 5-6 of the previous Office Action (03 August 2006) is *withdrawn* in view of amended and cancelled claims (12 March 2007).

6. The rejection of claim 13 under 35 U.S.C. §103(a) as set forth at pages 6-8 of the previous Office Action (03 August 2006) is *withdrawn* in view of the cancellation of this claim (12 March 2007).

7. The supplemental information disclosure statement filed on 16 March 2007 has been considered.

Information Disclosure Statement

It is noted that two of the references cited on the information disclosure statement of 16 March 2007 have been crossed off by the Examiner because they have been cited in duplicate (U.S. Patents 5,869,451 and 6,060,052).

However, the information disclosure statement filed 16 March 2007 also fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. *Specifically, the Examiner was unable to locate a copy of Bernard et al. (L'Inserm 33: 145-146, 1991).*

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claim 34 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described

in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 34 is directed a method of providing hematopoietic stem cells to a subject wherein said subject is treated with radiation therapy.

The specification as originally filed does not provide adequate written description for a method of providing hematopoietic stem cells to a subject wherein said subject is treated with radiation therapy. It is not expressly asserted, nor does it flow naturally from the specification. It is noted that the specification of the instant application only discloses that "the present invention can also reduce the proportion of subjects who are unable to harvest enough cells to proceed with treatment for their primary illness, e.g., chemotherapy and other bone marrow ablative treatments" (page 8, lines 6-10).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

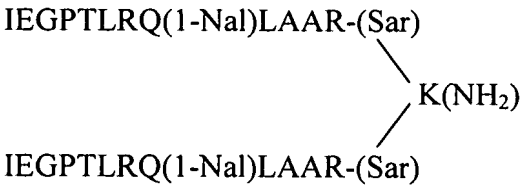
the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 2-12 and 15-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fibbe et al. (U.S. Patent 6,013,067) in view of Dower et al. (U.S. Patent 5,869,451). The basis for this rejection is set forth at pages 6-8 of the previous Office Action of 03 August 2006.

Fibbe et al. teach a method for increasing platelets or erythrocytes and a method for stimulating platelet or erythrocyte recovery in a patient comprising (1) administering to a donor an amount of TPO sufficient to stimulate proliferation of cells of the myeloid lineage, (2) collecting bone marrow cells or peripheral blood stem cells from the donor, and (3) administering the bone marrow cells or peripheral blood stem cells to a recipient patient (col 1, lines 55-63; claims 1, 13, for example). Fibbe et al. disclose that cells of the myeloid lineage include CD34+ stem cells and cells derived from CD34+ stem cells (col 4, lines 1-7). Fibbe et al. teach that the donor and recipient may be different individuals or the same individual (col 1, lines 63-64). Fibbe et al. also teach that bone marrow cells may be collected from the patient prior to chemotherapy or radiation therapy and returned to the patient subsequent to the therapy (col 2, lines 16-21). Fibbe et al. teach that collected marrow cells are cryopreserved according to established procedures and thawed prior to use (col 3, lines 60-65). Fibbe et al. teach that the use of allelic and engineered variant TPOs is contemplated, as well as truncated forms of TPO (col 3, lines 8-20).

Fibbe et al. does not teach that the TPO mimetic compound utilized in the method has reduced immunogenicity relative to one or more of rhTPO and rhIL-11 or that the compound has an improved PK profile relative to one or more of rhTPO and rhIL-11. Fibbe et al. does not teach any specific TPO mimetic sequence other than TPO. Fibbe et al. does not teach that the TPO mimetic compound is covalently attached to a hydrophilic polymer.

Dower et al. teach TPO mimetic compounds that have strong binding properties to the TPO receptor and that can activate the TPO receptor. For example, Dower et al. disclose TPO mimetic compounds with the following sequences : IEGPTLRQWLAAR-Sar (SEQ ID NO: 215) and IEGPTLRQ(1-Nal)LAAR-Sar (SEQ ID NO: 216) (col 5, 57-58; claim 1). Dower et al. disclose that synthetic amino acids, such as naphthylalanine, can be substituted for tryptophan, facilitating synthesis (column 29, lines 30-36). Dower et al. teach that preferred synthetic amino acids include L-(1-naphthyl)-alanine (1-Nal) and L-(2-naphthyl)-alanine (2-Nal) (column 15, lines 8-15). Dower et al. disclose that peptide compounds may be dimerized or oligomerized to increase the affinity and/or activity and disclose a TPO mimetic compound with the formula (col 5, 57-58; claim 1):



Dower et al. teach that the TPO peptides may be covalently attached to one or more hydrophilic polymers, including polyethylene glycol (bottom of col 5 through top of col 6; col 33, lines 4-25). Dower et al. discloses that when peptide compounds are derivatized with a

hydrophilic polymer, their solubility and circulation half-lives are increases and their immunogenicity is masked (col 32, lines 39-46). Dower et al. continues to teach that hydrophilic polymers have an average molecular weight ranging from about 500 to about 100,000 daltons, more preferably from about 2,000 to about 40,000 daltons, even more preferably from about 5,000 to about 20,000 daltons (col 32, lines 55-62). Dower et al. also teach that several PEGylated TPO peptides have an increased pharmacokinetic profile (col 59-62).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the method for increasing platelets or erythrocytes and the method for stimulating platelet or erythrocyte recovery in a patient as taught by Fibbe et al. by utilizing the TPO mimetic compound as taught by Dower et al. The person of ordinary skill in the art would have been motivated to make that modification because peptide mimetics have advantages over polypeptides, such as more economical production, greater chemical stability, altered specificity, enhanced pharmacological properties, and reduced antigenicity (see Dower et al.; col 14, lines 13-19). The person of ordinary skill in the art reasonably would have expected success because peptide mimetics of other receptor-binding peptides were already being generated and utilized in methods at the time the invention was made. Therefore, the claimed invention as a whole was clearly *prima facie* obvious over the prior art.

At page 10 of the Response, Applicant asserts that the '067 patent does not disclose or suggest the use of the TPO mimetics such as that presently claimed. Applicant also argues that neither the '067 patent nor the '451 patent disclose or suggest the use of the particularly claimed compound in a method of providing hematopoietic stem cells to a subject such as that claimed.

Applicant's arguments (12 March 2007), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references (see rejection above). See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Additionally, regarding Applicant's contention that neither reference discloses or suggests the use of the claimed TPO compound of the instant claims, Dower et al. disclose TPO mimetic compounds with the following sequences : IEGPTLRQWLAAR-Sar (SEQ ID NO: 215) and IEGPTLRQ(1-Nal)LAAR-Sar (SEQ ID NO: 216) (col 5, 57-58; claim 1). Dower et al. disclose that synthetic amino acids, such as naphthylalanine, can be substituted for tryptophan, facilitating synthesis (column 29, lines 30-36). *Dower et al. explicitly teach that preferred synthetic amino acids include L-(1-naphthyl)-alanine (1-Nal) and L-(2-naphthyl)-alanine (2-Nal) (column 15, lines 8-15).* Since the only difference between 1-Nal and 2-Nal is the position where alanine is attached to naphthalene, these compounds are homologs. It is noted that MPEP § 2144.08 (II)(A)(4)(c) states that "[i]f such a species or subgenus is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties. See, e.g., *Dillon*, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also *Deuel*, 51 F.3d at 1558, 34 USPQ2d at 1214 ("Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of

ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."). Thus, the claimed invention of the instant application as a whole was clearly *prima facie* obvious over the prior art.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BEB
Art Unit 1647
03 May 2007

Bridget E. Bunner

BRIDGET BUNNER
PATENT EXAMINER